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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,882	08/17/2005	Michael Lyne	GJE-7477	1606

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
03/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,882	LYNE, MICHAEL	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 31, 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed December 31, 2007 have been received and entered into the application.

Action Summary

The rejection of claims 2-9 under 35 U.S.C. 103(a) as being unpatentable over Fasmer et al. (1987) in view of Williams et al. (WO02/00195 A2) is being maintained for the reasons stated in the previous Office Action.

Response to Arguments

Applicant's arguments filed December 31, 2007 have been fully considered but they are not persuasive. Applicant argues that although it is true that (+)-nefopam was previously known as an analgesic, there is nothing in the cited references suggesting the advantageous utility of the claimed composition for intranasal administration as claimed. This is not found persuasive because Fasmer et al. teaches that the antinociceptive activity of (+)-nefopam was significantly more portent than (-) nefopam, and Williams et al. teach that nefopam compound is suitable for the application to the mucous membrane of the nasal cavity. Therefore, it would have been obvious to one of ordinary skill in the art to employ (+) nefopam for application to intranasal cavity for the

treatment of pain because (+)-nefopam has advantage over (-)nefopam having significantly potent analgesic activity as taught by Fasmer and nefopam compound is suitable for intranasal application as taught by Williams et al. Applicant argues that Williams et al. reference discloses nefopam (the racemate) as one of a long list of analgesics over 100 analgesics. This is not persuasive because Williams et al. teach that analgesic compositions that are useful for long-lasting pain relief from mucosal damage of the nasal cavity are preferred to be administered directly to the nasal cavity including nefopam composition. Therefore, one would have been motivated to employ (+)-nefopam taught by Fasmer et al. that is more potent form of nefopam in order to achieve long-lasting pain relief from mucosal damage in nasal cavity by intranasal administration as taught by Williams et al. Further, Williams et al.'s long list of analgesics of intranasal administration teach that intranasal administration is routine and commonly applied to many of analgesic agents for the treatment of pain including nefopam compound. Applicant argues that it would not be obvious to use each and every one of the thousands of compound mentioned by Williams et al. (including each and every enantiomer) or intranasal administration and therefore, the Office Action must identify additional teachings that would direct the person skilled in the art to the particular advantageous composition and use claimed by the current applicant. This is not found persuasive because the Office Action provided support for the position that nefopam compound is suitable for intranasal mucosal application in view of Williams et al. The Applicant provides no reason why William et al's teaching of the compounds disclosed by Williams et al. can not be administered intranasally. Applicant argues that

William et al. described administration to treat a local problems, i.e. mucosal inflammation, but the compositions and method of the subject invention advantageously deliver significant concentrations of (+)-nefopam to the central nervous system (CNS) with reduced side-effects. This is not found persuasive because Williams et al. teach compositions useful for long-lasting pain relief that are suitable for intranasal application. Further, Applicant's alleged reduced CNS side-effects by administration of intranasal (+)-nefopam is conjecture without the supporting data. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

It is suggested that Applicants submit a declaration to clearly establish a surprising and unexpected result using Applicants teaching.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fasmer et al. (1987) of record in view of Williams et al. (WO02/00195 A2) of record.

Fasmer et al. teach the antinociceptive effects of (+)-nefopam in mice. (abstract). Fasmer et al. teach that the antinociceptive activity of (+)-nefopam was significantly more potent than (-)-nefopam. (abstract). **Fasmer et al. teach that (+)-nefopam was**

dissolved in 0.9% NaCl. (page 508, under materials and methods). Fasmer's teaching of 0.9% **NaCl** to dissolve (+)-nefopam anticipates the claimed limitation of the "solubility enhancer" set forth in claim 3 because NaCl combined with (+)-nefopam promotes the dissolution of (+)-nefopam.

Fasmer et al. teach the antinociceptive effects of (+)-nefopam in mice. (abstract). Fasmer et al. teach that the antinociceptive activity of (+)-nefopam was significantly more potent than (-)-nefopam. (abstract). Fasmer et al. teach that (+)-nefopam was dissolved in 0.9% NaCl. (page 508, under materials and methods). Fasmer et al. teach that nefopam is an effective analgesic in man and its **analgesic activity** can also be demonstrated in some of **tests of nociception** in animals. (page 508, left-hand column). Fasmer et al. teach in conclusion, that (+)-nefopam is more potent as an **analgesic** than the (-) enantiomer. (page 511, right-hand, column, 3rd full paragraph).

Fasmer et al. do not teach the intranasal administration for treatment of pain set forth in claims 4, pain associated with cancer set forth in claim 8, the amount of (+) nefopam set forth in claim 9, the other agents set forth in claim 6, and the pH ranges set forth in claims 2,4 and 7.

Williams et al. teach that the composition comprising **nefopam** is suitable for application to the mucous membrane of the nasal cavity to relieve pain. (page 12, line 16, abstract). Williams et al. teach that the **painful condition** and symptoms are endured by almost all **chemotherapy** patients. (page 1, lines 23-25). Williams et al. teach that the composition is preferably applied to a mucosal surface of the subject's nasal cavity. (page 3, lines 10-13). Williams et al. teach that the **pH** of the composition

is within the range of from about **2 to about 9**, more preferably, about **3 to 7**, even more preferably **about 4 to about 5**, and optimally about **4.5**. (page 10, lines 26-28). These ranges encompasses and/or overlap and/or within Applicant's pH set forth in claims 2, 4 and 7. Williams et al. teach that **NMDA receptor antagonists**, a **non-steroidal anti-inflammatory agents**, **local anesthetics**, and **narcotic analgesics (opioids)** can be included in the composition and also suitable for application to nasal mucous cavity. (page 4, page 11, examples). Williams et al. teach that **mucoadhesives** can be also employed in the composition (page 7, lines 8-15).

It would have been obvious to one of ordinary skill in the art to modify the (+) nefopam formulation taught by Fasmer et al. to intranasal administration for treatment of pain because Williams et al. teach that nefopam comprising formulation in general are preferably applied directly to nasal cavity. One would have been motivated to make such a modification in order to employ preferred route of administration of nefopam known in the art as taught by Williams et al. It would have been obvious to one of ordinary skill in the art to adjust the pH of (+) nefopam formulation within about 3 to 7, even more preferably about 4 to 5 because Williams et al. teach the pH of nefopam suitable for intranasal application. One would have been motivated to optimize the pH of (+) nefopam suitable for intranasal application taught by Williams et al. in order to avoid any irritation in nasal cavity. It would have been obvious to one of ordinary skill in the art to further include other agents such as NMDA antagonist, non-steroidal anti-inflammatory agents set forth in claim 6, because these agents are also effective for the treatment of pain and suitable for the nasal mucosal application as taught by Williams et

al. One of ordinary skill in the would have been motivated to combine the agents set forth in claim 6, in order to achieve at least an additive effect in treatment of pain. It would have been obvious to one of ordinary skill in the art that Fasmer et al's (+) nefopam formulation as modified by Williams et al. is effective to treat pain including pain associated with cancer because Fasmer et al. teach that (+) nefopam is more potent as an analgesic than its enantiomer and because almost all cancer patients endure pain. There is a reasonable expectation of successfully treating pain associated with cancer with (+) nefopam nasal composition because (+) nefopam possess not only effective analgesic property but significantly more potent than its enantiomer, (-) nefopam, in man. Further, the nasal applicability of nefopam in general is well taught by Williams et al. with its suitable pH. The amount of (+) nefopam to be employed set forth in claim 9 is obvious because Fasmer teaches that nefopam is an effective analgesic agent in man. One would have been motivated to optimize the effective analgesic amounts in man as taught by Fasmer et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
March 18, 2008